IV. RESPONSE TO RESTRICTION REQUIREMENT

In the present Office Action, the Examiner takes the position that, with respect to claims 10, 11, 21, 22, 34, 61 and 62, Applicants have presented claims in improper Markush format and cites to *Ex parte Markush*, 1925 C.D. 126 and *In re Weber*, 198 U.S.P.Q. 334 as legal support for this position. The Examiner's argument also relies upon 35 U.S.C. § 121 as statutory support for this restriction requirement. However, the proper citation to *In re Weber* is 580 F.2d 455, 198 U.S.P.Q. **328** (CCPA, 1978). Nevertheless, the case cited at 198 U.S.P.Q. 334 (*In re Haas*) does pertain to same question or law.

Applicants hereby respectfully traverse the present restriction requirement as being clearly contrary to the express holding of both *In re Weber* and *In re Haas*. *In re Weber* expressly holds that:

> It is apparent that § 121 provides the Commissioner with the authority to promulgate rules designed to Restrict an Application to one of several claimed inventions when those inventions are found to be "independent and distinct". It does not, however, provide a basis to an examiner acting under the authority of the Commissioner to Reject a particular Claim on that same basis. *In re Weber*, 580 F.2d 455, 458, 198 U.S.P.Q. 328, __, (CCPA, 1978)
>
> **We hold that a rejection under § 121 violates the basic right of the applicant to claim his invention as he chooses** (emphasis added). *In re Weber*, 580 F.2d 455, 459, 198 U.S.P.Q. 328, __, (CCPA, 1978)

Accordingly, it is clear from the precedent cited by The Office, the legal issue of whether or not The Office may impose a restriction requirement to a single claim has been decided against The Office. It is well settled that such a requirement violates 35 U.S.C. 112, where the applicant is statutorily entitled to claim his invention as he deems proper notwithstanding 35 U.S.C. § 121. This is true whether or not the inventions are determined by The Office to be independent and distinct.

Applicants further note that in each Group that the Examiner argues is a separate invention (each distinct Seq. ID No. (e.g. 1-11)) is classified in Class 435, subclass 6 and Class 536, subclass 24.32. Thus, for purposes of a search, there is no additional burden on The Office since the same class and subclasses must be searched, and no additional Class or subclass must be searched, whether or not a restriction requirement is imposed.

Additionally, Applicants take the position that said claims are generic and use proper Markush format. Accordingly, Applicant takes the position that the present restriction requirement is improper and therefore request that it be withdrawn.

Because the rules REQUIRE that an election be made by Applicant's, notwithstanding any traverse of a restriction requirement, the provisional election of Group I probes to Seq. ID. No. 1 (made no April 26, 2001) is hereby reaffirmed. However, because Applicants traverse the restriction requirement, no amendment or cancellation of claims has been offered in this response as Applicants reserve their right to appeal said restriction requirement. Hence, Applicant's consider all of claims 1-34, 46-49, 60-62, 72 and 80-85, as amended herein for other purposes, as being presently pending.

V. RESPONSE TO SEQUENCE LISTING/SPECIFICATION OBJECTION

The Examiner has objected to the specification, apparently taking the position that not all of the properly reportable sequence information has been included in the sequence listing as required under 37 C.F.R. §1.821(d). In particular the Examiner makes reference to page 29 of the specification, and presumably to the information in Table 2. Applicants respectfully submit that the Sequence Listing is in absolute compliance with 37 C.F.R. § 1.821 as the information in Table 2 is not required to be input to the Sequence Listing by the express language of the Rule.

The information in Table 2 of Applicant's specification identifies peptide nucleic acid (PNA) probes that were actually prepared. The confusion here appears to lie in a general misunderstanding. Specifically, the Examiner appears to believe that a peptide

nucleic acid is either a nucleic acid a peptide and therefore must be disclosed in the sequence listing. It, however, is well established that a peptide nucleic acid is neither a nucleic acid nor a peptide.

The express rule of 37 C.F.R. § 1.821 states that: "Nucleotides and/or amino acid sequences as used in §§ 1.821-1.825 are interpreted to mean an unbranched sequence of four or more amino acids or an unbranched sequence of ten or more nucleotides. The terms Nucleotide and Amino acid are further expressly defined by the rule. In particular, Nucleotides "are intended to embrace **ONLY** those nucleotides that can be represented using the symbols set forth in WIPO Standard ST.25 (1998) ...(emphasis added)" Likewise, amino acids are those L-amino acids commonly found in naturally occurring proteins and are listed in WIPO Standard ST.25 (1998)...".

It is well accepted that PNA is composed of achiral amino acid monomers, none of which are set forth in WIPO Standard ST.25. Moreover, it is well established that PNA is not composed of nucleotides since, by definition, a nucleotide comprises a sugar unit, a phosphorus moiety and an nucleobase. Accordingly, the nucleotide symbols in WIPO standard ST.25 are not appropriate. Thus, it is clear that any specific PNA probe need not be properly listed in a Sequence Listing as per the express language of the Rules (i.e. 37 C.F.R. §1.821-1.825). **If the Examiner disagrees with this argument, it is requested that the Examiner specify whether the rules for Nucleotides or rules for amino acids apply to PNA oligomers and specifically why.**

VI. RESPONSE TO OTHER REJECTIONS

i) Rejections Under 35 U.S.C.§112, second paragraph

It is believed that the amendments set forth above will cure all of the objections to the claims (See: page 5 of the Office Action) and the rejections set forth under 35 U.S.C. §112, second paragraph (See: paragraph 4 of the Office Action at pages 6-10) except for the following. In particular, Applicants traverse the articulated rejection of claims 46-49, 60-62 and 80-85 as set forth at the top of page 9 of the present Office Action

as well as the rejection of claims 80-82 as forth at the bottom of page 9 of the present Office Action.

With respect to claims 46-49,60-62 and 80-85 it is well settled that a claim is sufficiently definite for purposes of the second paragraph of 35 USC § 112 if one of ordinary skill in the art would understand what is claimed when considered in light of the specification and the prior art. *Penda Corporation v. United States*, 29 Fed.Cl. at 554. There is no requirement that the specification list every parameter of operation, so long as those of ordinary skill in the art realize that the parameter may be readily obtainable *Id.* Patent claims are not required to set forth design parameters specific to every conceivable situation involving the claimed invention. *Chemcast Corp. v. Arco Industries Corp.*, 854 F.2d 1328, 1988 WL 76528 **3 (Fed.Cir. (Mich.)). This is true even where some experimentation is required, so long as the experimentation is not undue. *Penda*, 29 Fed.Cl. at 554.

The claims at issue recite that hybridization occurs under "suitable *in-situ* hybridization" conditions. Said conditions are defined in the specification at page 13, lines 25-37 with reference to achieving a desired degree of discrimination such that the assay generates an accurate and reproducible result. Parameters most often varied by those of skill in the art to adjust stringency are also discussed in the specification beginning at page 13, lines 11-23. Furthermore, it is respectfully submitted that the art of hybridization is so well developed that clearly one of skill in the art would most certainly appreciate how to achieve suitable hybridization conditions to achieve an accurate and reproducible result. It is therefore respectfully submitted that, taken as a whole, the teachings of the specification and the knowledge of the ordinary practitioner when applied to the claims and specific reference to the language "suitable hybridization conditions" or "suitable *in-situ* hybridization" renders the claims sufficiently definite for compliance with 35 USC § 112, second paragraph, with respect to "the specificity of the probe for hybridization". Therefore, withdrawal of this rejection is requested.

With respect to claims 80-82, the Examiner argues that is it unclear as to whether the reagents of a)-h) are considered to be the "reagents or compositions necessary to perform the assay or whether the reagents are present in addition to the "reagents or compositions necessary to perform the assay". It is respectfully submitted that this question need not be answered for the claim to be definite.

Claim 72 recites a kit **comprising** certain components. Comprising is well accepted as being an open ended term such that additional elements may be present and still infringe the claimed subject matter. Such claim format is well established as being definite. Hence, any dependent claim, such as claims 80-82, may recite elements that are in addition to those specified by the independent claim 72. Like claim 72, claims 80-82 pertain to kits **comprising** certain recited elements or optional elements. Accordingly, there is no requirement that dependent claims, such as 80-82, distinguish between elements necessary to perform an assay and those which are optional, as apparently the Examiner feels is required. Thus, Applicants respectfully request that such rejection be withdrawn.

Additionally the Examiner suggests that it is unclear as to whether or not "the soybean labeled probe of e) is present in addition to the "one or more *Dekkera/Brettanomyces* specific probes" as recited in a) of claim 80". It is believed that the Examiner is referring to a) of claim 72 and not claim 80. Nevertheless, it is clear from claim 72 that at least one probe of the type set forth in e) of claim 80 is required to perform the assay and therefore qualifies as a probe satisfying the requirements of a) of claim 72. Thus, the confusion expressed by the Examiner is certainly not well understood. Moreover, it is believed that the claimed subject matter is clear within the requirements of 35 U.S.C. §112, second paragraph.

In view of the foregoing remarks and amendments, it is respectfully submitted that all of the presently applied rejections under 35 U.S.C. §112, second paragraph should properly be withdrawn.

ii) Rejections under 35 U.S.C. § 102

(a) Rejection in view of Stender et al. under 35 U.S.C. §102(a)

The Examiner is thanked for acknowledging (at page 11 of the Office Action) that although the inventorship of the present application differs from the authorship of the cited reference, such rejection can be overcome by the filing of an appropriate declaration. Enclosed with the papers accompanying the present application is an appropriate Declaration under 37 C.F.R. §1.131. Accordingly it is believed that the rejection of claims 1-7, 9, 12, 14, 15, 20, 23, 24, 26-28, 33, 46-49, 60 and 83-85 under 35 U.S.C. §102(a) as being anticipated by Stender et al. (Abstracts of the General Meeting of the American Society for Microbiology, May 30-June 3, 1999, page 516) is rendered moot and accordingly should be withdrawn.

(b) Rejection in view of Kosse (reference DF) under 35 U.S.C §102(b)

It is well accepted that in order to anticipate claimed subject matter, a single reference must disclose each and every claim element. It is respectfully submitted that independent claims 9, 20, 33 and 60 have been amended to include the element/limitation that the probes be enzyme-linked. As Kosse describes only fluorescently labeled probes, it does not disclose all of the elements of the presently claimed subject matter. Accordingly, it is submitted that the present rejection of claim 9, 14, 15, 17, 20, 23, 24, 27, 28, 30, 33 and 60 under 35 U.S.C. § 102(b) should be withdrawn.

(c) Rejection in view of De Wachter et al. (GenBank Accession No. X58052)

As discussed above, independent claim 9 has been amended to include the element/limitation that the probe is enzyme-linked. Accordingly, it is submitted that De Wachter et al. does not teach of the elements/limitations of the presently rejected claims. Accordingly, it is submitted that the present rejection of claims 9-11 and 13 under 35 U.S.C. § 102(b), as being anticipated by De Wachter, should be withdrawn.

iii) Rejections under 35 U.S.C. § 103(a)

(a) Rejections based upon Stender et al. (1999)

At paragraphs 8 and 9 of the present Office Action (pages 13-16), Stender et al. (Abstracts of the General Meeting of the American Society for Microbiology, May 30-June 3, 1999, page 516) is used alone or in combination to reject claim 72 as well as claims 8, 13, 16-19, 25, 29-32 and 80-82. In view of the present Declaration under 37 C.F.R § 1.131, included herewith, it is respectfully submitted that these rejections should be withdrawn as said publication by Stender et al. is disqualified as an available reference against the presently claimed subject matter.

(b) Rejection based upon Kosse

At paragraph 10 of the present Office Action, the Examiner has rejected claim 72 as being unpatentable over Kosse et al. (*Systems. Appl. Microbiol. 20:* 468-480 (1997). The Examiner apparently takes the position that Kosse et al. teaches *in-situ* hybridization methods for the detection of *Dekkera bruxellensis* using fluorescently labeled probes and that, although not expressly taught by Kosse, the packaging of reagents into kits for *in-situ* hybridization is *prima facie* obvious.

Claim 72 has been amended to include limit the scope of the claim to enzyme-linked probes. As Kosse et al. does not teach enzyme-linked probes, it is respectfully submitted that the present rejection should be withdrawn as the cited reference does not teach all of the elements/limitation of the presently claimed subject matter.

(c) Rejection based upon Kosse and Stender (1998)

At paragraph 11 of the present Office Action, the Examiner has rejected claims 1-8, 12, 13, 16, 18, 19, 25, 26, 29, 31, 32, and 46 under 35 U.S.C. §103(a) as being unpatentable under Kosse in view of Stender (1998). However, careful reading of the argument made in support of this rejection reveals that the Examiner is also relying heavily upon Stender et al. (1999). As Stender (1999) cannot be used to reject the presently pending claims in view of the Declaration under 37 C.F.R. § 1.131 submitted herewith by Applicants, it is submitted that some or all of the foregoing rejection should be withdrawn.

Notwithstanding the foregoing, while Kosse et al. teaches methods for the detection of *Dekkera Bruxellensis* yeast using fluorescently labeled probes and Stender (1998) teaches the detection of bacteria (not yeast) using labeled probes that include enzyme labeled probes, no art cited by the Examiner in support of the present rejection teaches the analysis of yeast using enzyme-linked probes, such as soy bean peroxidase labeled probes. This is significant because, as discussed by Applicants at page 3, line 30 to page 4, line 6, it is likely difficult to get such large molecules to pass through the cell membrane and into the cytoplasm of the yeast cell.

This position is supported by the express teaching of Amann et al. (**Identification of individual prokaryotic cells by using enzyme-labeled, rRNA-targeted oligonucleotide probes**, *Applied and Environmental Microbiology, 58:* 3007-3011 (1992), Reference CA). According to the abstract, Amann et al. were able to perform *in-situ* hybridization analysis, using enzyme-linked nucleic acid probes, of gram-negative bacteria and archaebacteria, but were unable to perform similar analysis of gram-positive bacteria or yeast cells using said enzyme-linked probes. According to the background (page 3007, col. 2, lines 3-7), the limitations imposed by the size of a probe are discussed with respect to its ability to penetrate the cell wall and thereby be an effective agent for analysis. In the section entitled "Penetration of HRP-labeled oligonucleotides into whole cells" (pages 3008-3010) there is an extensive discussion of the successes and failures encountered by Amann et al. In particular they note that the size/weight of the probe, caused by the large enzyme molecule, is a limiting factor that prevents the use of enzyme-linked probes for the analysis of yeast species, such as *Dekkera Bruxellensis*. Thus, Amann et al. stands as a substantial **teaching away** from that which the Examiner believe is *prima facie* obvious; i.e. the substitution of an enzyme-linked probe for a fluorescently labeled probe for the analysis of yeast.

In view of the foregoing remarks, as well as the amendment to independent claims 9 and 20, it is respectfully submitted that the present rejection of claims 1-8, 12, 13, 16, 18, 19, 25, 26, 29, 31, 32 and 46 under 35 U.S.C. §103(a) should be withdrawn.

(d) Rejection based upon Kosse in view of Stender (1998) and Parton

At paragraph 12 of the present Office Action (page 20), the Examiner has rejected claims 47, 48 and 80-85 as being unpatentable over Kosse in view of Stender (1998) and in further view of Parton (US Patent No. 5,905,038). Apparently the Examiner takes the position that the combination of Kosse and Stender is properly supported and that Parton provides elements not found in the prior articulated rejection.

With respect to claims 47 and 48, Applicant's take the position that Amann provides an appropriate **teaching away** so as to overcome the rejection of independent claim 46 (discussed above). Accordingly dependent claims 47 and 48 cannot be rejected in view of Kosse, Stender and Parton. Similarly with respect to claims 80-85, the claimed subject matter pertains to the analysis of yeast using enzyme-linked probes. Thus, it is believed that the combination of references is improper based upon the teachings of Amann et al. Therefore, it is respectfully submitted that this rejection should be withdrawn.

(e) Rejection based upon De Wachter in view of Kosse

At the first paragraph 13 (page 21) of the present Office Action, the Examiner has rejected claims 14-15, 17, 20-24, 27, 28, 30, 33, 60-62 and 72 under 35 U.S.C. §103(a) as being unpatentable over De Wachter in view of Kosse.

In view of the amendments and remarks set forth above, it is believed that the identified claims are patentable over this combination of references. In particular, De Wachter merely discloses sequence information and therefore adds nothing to Kosse with respect to the analysis of yeast using enzyme-linked probes. Accordingly, it is respectfully submitted that the aforementioned rejection should be withdrawn in view of the amendments and remarks set forth herein.

(f) Rejection based upon De Wachter in view of Kosse and Stender (1998)

At the second paragraph 13 (page 23) of the present Office Action, the Examiner has rejected claims 12, 16, 18, 19, 25, 26, 29, 31 and 32 under 35 U.S.C. § 103(a) as being unpatentable over De Wachter in view of Kosse and further view of Stender et al (1998).

In view of the amendments and remarks set forth above, it is believed that the identified claims are patentable over this combination of references. In particular, De Wachter merely discloses sequence information and therefore adds nothing to Kosse with respect to the analysis of yeast using enzyme-linked probes. Additionally, Stender et al. (1998) is directed to the detection of bacteria and therefore does not address the difficulties articulated by Amann et al. with respect to the *in-situ* analysis of yeast using enzyme-linked probes. Accordingly, it is respectfully submitted that the aforementioned rejection should be withdrawn in view of the amendments and remarks set forth herein.

VII. SUMMARY

It is believed that this response addresses all rejections set forth in the present Office Action and the application is in ready condition for allowance. In consideration of the preceding amendments and remarks, Applicants hereby respectfully request reconsideration of all pending and added claims, the withdrawal of all rejections set forth in the present Office Action and issue of a Notice of Allowance by The Office.

VIII. INTERVIEW

If the Examiner believes a telephonic or personal interview would advance the prosecution of the subject application, the Examiner is invited to contact attorney Gildea during business hours at the telephone or facsimile numbers listed below.

IX. ENCLOSURES

1. Petition under 37 C.F.R. § 1.136(a) for a three month extension of time
2. Declaration under 37 C.F.R. § 1.131

X. FEES

Except for the fee due for consideration of the petition under 37 C.F.R. §1.136(a), it is believed that no additional fees are believed due The Office for consideration of this

paper. If however, The Office determines that any other fee is due, authorization is hereby granted to charge any required fee associated with the filing and consideration of this paper to Deposit Account 02-3240.

XI. CORRESPONDENCE/CUSTOMER NUMBER

Please send all correspondence pertaining to this document to:

Boston Probes, Inc.
Attn: Brian D. Gildea, Esq.
15 DeAngelo Drive
Bedford, MA 01730

Telephone: 781-280-2824
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IF NOT ALREADY DONE, PLEASE MATCH THIS CASE WITH CUSTOMER NUMBER **23544**

[Insert Customer Number Bar Code]

Respectfully submitted
on behalf of Applicants,

Brian D. Gildea, Esq.
Reg. No. 39,995